Remarks

Applicants affirm the election of the claims of Group I wherein W is carbocyclic aryl, Ar is thienyl and Q is pyridyl. Applicants note that upon conferring with the examiner in an informal teleconference, the examiner stated that the description of the compounds of species I in the restriction requirement erroneously included the statement "Q is pyrimidine." Consequently, the applicants have amended the claims so that Q is an optionally substituted pyridyl. However, the applicants respectfully request the examiner to reconsider the Restriction Requirement. Searching all the various groups originally encompassed by the definition of Q would not be unduly burdensome. Specifically searching the thienopyridine core wherein W is carbocyclic aryl without limiting Q to pyridyl would not be an undue burden. Consequently, the applicants request that the definition of Q should be broadened to cover all heteroaryl groups.

Claims 2-8, 10, 13, 17, 20-26, 29, 35, 36, 38, 39, 41-44, 52, and 71-73 have been cancelled without prejudice to the filing of continuing applications. Claims 1, 11, 15, 18, 19, 53, 56-59, and 63-70 have been amended.

The structure in claim 1 was amended to correct a typographical error. Specifically, in formula I, $(CH_2)_n$ was

replaced by the variable "X." Support for this amendment can be found within claim 1 where "X" was originally defined while the variable "X" did not appear in the structure. Additionally, as noted on pages 11-12, specific compounds of the invention include compounds of Formulas III, IV, and VII, all of which contain the variable "X." It should be noted that in these formulas, "X" is defined as in formula I. Consequently, it is clear that formula I contains a typographical error and $(CH_2)_n$ can properly be replaced by the variable "X." No new matter is added by this amendment.

Furthermore, in claim 1, the word "heterocycloalkyl" was misspelled as "heteroacycloalkyl." This typographical error was corrected. No new matter is added by this amendment.

Claims 56-59 have been amended to correct a typographical error. These claims are method claims that originally improperly depended from composition of matter claims 40, 41, or 43. As amended, claims 56-58 depend from method claim 54. Claim 59 as amended depends from claim 58. No new matter is added by this amendment.

Claims 63-66 have been amended to correct a typographical error, and now depend from independent method claim 62. Support for these amendments is evident upon reviewing claims 62-66. No new matter is added by these amendments.

Claims 67-70 have been amended to correct a typographical error, and now depend from claim 53. Support for this amendment

is found in the claims and on page 21, lines 1-11. No new matter is added by this amendment.

Rejection under 35 U.S.C. §112

Claims 1 and 9-62 stand rejected because the specification allegedly does not enable compounds wherein W encompasses all heteroaryl or heterocycloalkyl groups. The Applicants have amended the claims only pursuant to the restriction requirement, and not at all for reasons related to the 35 U.S.C. §112 rejection. The limitation of W to carbocyclic aryl is not meant to be an acquiescence in the rejection under §112. Indeed, Applicants disagree with the §112 rejection directed to the definition of W. This rejection should be withdrawn.

Claims 54-66 stand rejected because the specification allegedly fails to teach how to use the claimed invention. In particular, the examiner argues that these claims are rejected because the method for altering signal transduction allegedly has no practical utility. Applicants respectfully submit that one of skill in the art would appreciate that there are situations, both in the context of disease therapy and *in vitro* therapy, in which one would wish to alter signal transduction. For example, in a patient, alteration of GABA-induced signal transduction may be beneficial in the treatment of various CNS disorders. See for example, pages 19-20 of the specification as

filed, which list many conditions that can be treated by altering GABA-induced signal transduction.

Moreover, *in vitro* alteration of signal transduction has utility in assessing activity of a candidate compound or in the identification of additional therapeutic agents. See Example 31 which illustrates such a use; specifically, the alteration of signal transduction is assessed using electrophysiological techniques for the purpose of evaluating activity of a candidate compound.

The lack of specific diseases that can be treated using such alteration is also cited by the Examiner as proof of lack of utility. Applicants submit that the diseases to be treated include those listed on pages 19-20 of the specification. Furthermore, as stated above, such alteration is also useful in finding agents for the treatment of such diseases. Consequently, it is clear that altering signal transduction is useful and has utility. Therefore, the applicants respectfully request that the Examiner withdraw the rejections of these claims based on 35 U.S.C. § 112.

Claim 53 stands rejected under U.S.C. § 112 for allegedly being indefinite. The examiner specifically points to the phrase "at least." Applicants believe that one of skill in the art would recognize that a pharmaceutical composition can contain at least one, i.e., one or more, carriers and/or

excipients. However, in order to expedite prosecution of the case, Applicants have amended the claim to delete the term in question and replaced it with the word "a." One of skill in the art will recognize that the scope of the claim has not been limited because claim 53 uses the phrase "comprising." Therefore, one of skill in the art will recognize that more than one carrier and/or excipient may be present.

Allowance of the claims and passage of the case to issue are respectfully solicited. Should the Examiner believe a discussion of this matter would be helpful, she is invited to telephone the undersigned at (312) 913-0001.

Respectfully submitted,

Dated: July 26, 2002 By: _____

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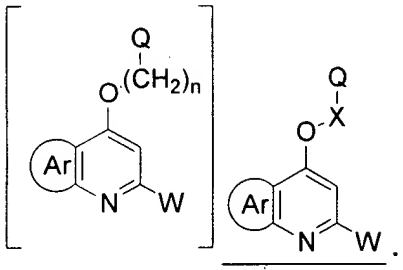
Version marked to show changes made

In the specification:

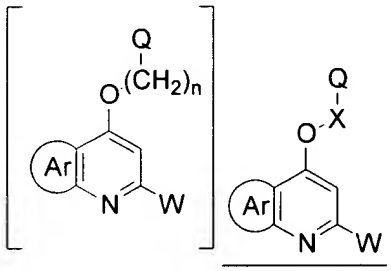
On page 5, line 25:

Delete the structure of formula I and replace it with the following structure:

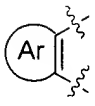


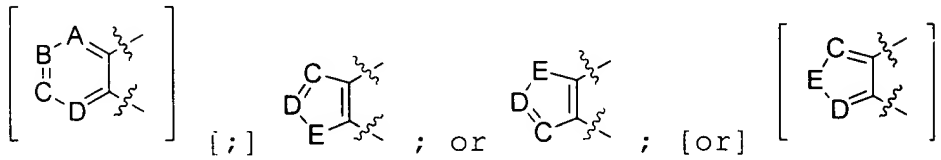
In the claims:

1. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

 represents:



wherein:

C and D are CR_1, and

E represents sulfur,

where

R_1, at each occurrence, is independently selected from the group consisting of hydrogen, halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, C_{1-6} alkyl, amino, mono and di(C_{1-6})alkylamino, and C_{1-6} alkoxy; and

R_2 is selected from the group consisting of hydrogen, halogen, cyano, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, hydroxy, C_{1-6} alkyl, amino, and mono or di(C_1-C_6)alkylamino;

W is aryl which is unsubstituted or substituted with one or more R_3; and

Q is pyridinyl, which is unsubstituted or substituted with one or more of R_4;

R_3 and R_4 at each occurrence are independently selected from the group consisting of hydrogen, halogen, hydroxy, $-OR_6$, $-NO_2$, $-CN$, $-SO_2NH_2$, $-SO_2NHR_6$, $-SO_2N(R_6)_2$, amino, $-NHR_6$, $-N(R_6)_2$, $-N(R_6)CO(R_6)$, $-N(R_6)CO_2(R_6)$, $-CONH_2$, $-CONH(R_6)$, $-CON(R_6)_2$, $-CO_2(R_6)$, $-S(R_6)$, $-SO(R_6)$, $-SO_2(R_6)$, and R_7, wherein

R_6, at each occurrence, is independently selected from the group consisting of C_{1-8} alkyl, C_{2-8} alkenyl,

C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, and C_{5-9} cycloalkynyl, each of which is unsubstituted or substituted with one or more substituents selected from the group consisting of hydroxy, oxo, halogen, amino, C_{1-8} alkoxy, and C_{1-8} alkyl,

R_7 at each occurrence is independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkenyl, C_{1-8} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, and C_{5-9} cycloalkynyl, each of which is unsubstituted or substituted with one or more substituents selected from the group consisting of hydroxy, oxo, halogen, $-OR_6$, C_{1-6}alkyl, $-NO_2$, -CN, $-SO_2NH_2$, $-SO_2NHR_6$, $-SO_2N(R_6)_2$, amino, $-NHR_6$, $-N(R_6)_2$, $-N(R_6)CO(R_6)$, $-N(R_6)CO_2(R_6)$, $-CONH_2$, $-CONH(R_6)$, $-CON(R_6)_2$, $-CO_2H$, $-CO_2(R_6)$, $-S(R_6)$, $-SO(R_6)$, $-SO_2(R_6)$, and NR_aR_b, wherein

each NR_aR_b independently forms a monocyclic or bicyclic ring each of which may contain one or more double bonds, or one or more of oxo, O, S, SO, SO_2, NH, or $N(R_2)$, wherein R_2 is defined above and independently selected at each occurrence; or

Q is a group of the formula NR_8R_9 wherein

R_8 and R_9 are independently hydrogen or R_7; or

R_8, R_9 and the nitrogen to which they are attached form a heterocycloalkyl ring having from 5 to 8 ring atoms and where 1 or 2 of the ring atoms are selected from N, S, O, with remaining ring members being carbon, CH or CH_2, which [heteroacycloalkyl] heterocycloalkyl ring is unsubstituted or substituted with one or more independently selected R_4 groups; and

X is $-(CH_2)_n-$ or $-(CH_2)_n(C=O)-$, wherein each n is independently 1, 2, or 3.

11. (Amended) A compound or salt according to Claim [10] 9, wherein W is phenyl, [or pyridyl, each of] which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C_{1-6}alkoxy, -nitro, -CN, $-SO_2NH_2$, $-SO_2NHR_2$, $-SO_2N(C_{1-6}alkyl)_2$, amino, $-NHC_{1-6}$alkyl, $-N(C_{1-6}alkyl)_2$, $-N(C_{1-6}alkyl)CO(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)CO_2(C_{1-6}alkyl)$, $-CONH_2$, $-CONH(C_{1-6}alkyl)$, $-CON(C_{1-6}alkyl)_2$, $-CO_2(C_{1-6}alkyl)$, $-S(C_{1-6}alkyl)$, $-SO(C_{1-6}alkyl)$, $-SO_2(C_{1-6}alkyl)$, and C_{1-6}alkyl optionally substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

15. (Amended) A compound or salt according to Claim [13] 12; wherein

Q is selected from phenyl, pyridyl, pyrimidinyl, pyrazolyl, triazolyl, imidazolyl, pyrrolyl, piperidinyl, and

pyrrolidinyl, each of which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C_{1-6}alkoxy, -CN, amino, mono- and di(C_{1-6})alkylamino, and C_{1-6} alkyl which is unsubstituted or substituted with 1 or more substituents independently chosen from hydroxy, oxo, amino, halogen, C_{1-6}alkyl, C_{1-6}alkoxy, and mono- and di(C_{1-6})alkylamino; and

W is phenyl [or pyridyl, each of] which is unsubstituted or substituted with from 1 to 3 substituents independently selected from: halogen, hydroxy, C_{1-6}alkoxy, -nitro, -CN, $-SO_2NH_2$, $-SO_2NHR_2$, $-SO_2N(C_{1-6}alkyl)_2$, amino, $-NHC_{1-6}$alkyl, $-N(C_{1-6}alkyl)_2$, $-N(C_{1-6}alkyl)CO(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)CO_2(C_{1-6}alkyl)$, $-CONH_2$, $-CONH(C_{1-6}alkyl)$, $-CON(C_{1-6}alkyl)_2$, $-CO_2(C_{1-6}alkyl)$, $-S(C_{1-6}alkyl)$, $-SO(C_{1-6}alkyl)$, $-SO_2(C_{1-6}alkyl)$, and C_{1-6}alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

18. (Amended) A compound or salt according to Claim [17] 16, wherein

W is phenyl [or pyridyl, each of] which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C_{1-6}alkoxy, -nitro, -CN, $-SO_2NH_2$, $-SO_2NHR_2$, $-SO_2N(C_{1-6}alkyl)_2$, amino, $-NHC_{1-6}$alkyl, $-N(C_{1-6}alkyl)_2$, $-N(C_{1-6}alkyl)CO(C_{1-6}alkyl)$,

$-N(C_{1-6}alkyl)CO_2(C_{1-6}alkyl)$, $-CONH_2$, $-CONH(C_{1-6}alkyl)$, $-CON(C_{1-6}alkyl)_2$, $-CO_2(C_{1-6}alkyl)$, $-S(C_{1-6}alkyl)$, $-SO(C_{1-6}alkyl)$, $-SO_2(C_{1-6}alkyl)$, and C_{1-6}alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

19. (Amended) A compound or salt according to Claim 18, wherein:

Q is [selected from phenyl,]pyridyl, [pyrimidinyl, pyrazolyl, triazolyl, imidazolyl, pyrrolyl, piperidinyl, and pyrrolidinyl, each of] which is unsubstituted or substituted with from 1 to 3 substituents independently selected from: halogen, hydroxy, C_{1-6}alkoxy, -CN, amino, mono- and di(C_{1-6})alkylamino, and C_{1-6} alkyl which is unsubstituted or substituted with 1 or more substituents chosen from hydroxy, oxo, amino, halogen, C_{1-6}alkoxy, and mono- and di(C_{1-6})alkylamino; [or

Q is a group of the formula NR_8R_9 wherein:

R_8 and R_9 are independently hydrogen or C_{1-6} alkyl which is unsubstituted or substituted with 1 or more substituents chosen from hydroxy, oxo, amino, halogen, and C_{1-6}alkoxy, and mono- and di(C_{1-6})alkylamino; or

R_8, R_9 and the nitrogen to which they are attached form a pyrrolidinyl or piperidinyl ring which is unsubstituted or substituted with from 1 to 3

substituents independently selected from halogen, hydroxy, C_{1-6}alkoxy, -CN, amino, mono- and di(C_{1-6})alkylamino, and C_{1-6} alkyl which is unsubstituted or substituted with 1 or more substituents chosen from hydroxy, oxo, amino, halogen, C_{1-6}alkoxy, and mono- and di(C_{1-6})alkylamino;] and

W is phenyl [or pyridyl, each of]which is unsubstituted or substituted with from 1 to 3 substituents independently selected from halogen, hydroxy, C_{1-6}alkoxy, -nitro, -CN, $-SO_2NH_2$, $-SO_2NHR_2$, $-SO_2N(C_{1-6}alkyl)_2$, amino, $-NHC_{1-6}$alkyl, $-N(C_{1-6}alkyl)_2$, $-N(C_{1-6}alkyl)CO(C_{1-6}alkyl)$, $-N(C_{1-6}alkyl)CO_2(C_{1-6}alkyl)$, $-CONH_2$, $-CONH(C_{1-6}alkyl)$, $-CON(C_{1-6}alkyl)_2$, $-CO_2(C_{1-6}alkyl)$, $-S(C_{1-6}alkyl)$, $-SO(C_{1-6}alkyl)$, $-SO_2(C_{1-6}alkyl)$, and C_{1-6}alkyl which is unsubstituted or substituted with one or more substituents independently selected from hydroxy, halogen, and amino.

53. (Amended) A pharmaceutical composition comprising a compound or salt according to Claim 1 combined with [at least one] a pharmaceutically acceptable carrier or excipient.

56. (Amended) A method according to Claim [40] 54 wherein the detectable alteration of the electrophysiology of the cell is a change in the chloride ion conductance of the cell.

57. (Amended) The method of Claim [41] 54 wherein the cell is recombinantly expressing a heterologous $GABA_A$ receptor and the alteration of the electrophysiology of the cell is detected by intracellular recording or patch clamp recording.

58. (Amended) The method of Claim [41] 54 wherein the cell is a neuronal cell that is contacted in vivo in an animal, the solution is a body fluid, and the alteration in the electrophysiology of the cell is detected as a reproducible change in the animal's behavior.

59. (Amended) The method of Claim [43] 58 wherein the animal is a human, the cell is a brain cell, and the fluid is cerebrospinal fluid.

63. (Amended) The method of Claim [48] 62 in which the cell or tissue sample is a tissue section.

64. (Amended) The method of Claim [48] 62 in which the detectable label is a radioactive label or a directly or indirectly luminescent label.

65. (Amended) The method of Claim [48] 62 in which each cell or tissue sample is a tissue section, the detectable label is a radioactive label or a directly or indirectly luminescent

label, and the detectable label is detected autoradiographically to generate an autoradiogram for each of the at least one samples.

66. (Amended) The method of Claim [48] 62 in which each measurement of the amount of detectable label in a sample is carried out by viewing the autoradiograms and the comparison is a comparison of the exposure density of the autoradiograms.

67. (Amended) A package comprising a pharmaceutical composition of claim [36] 53 in a container and further comprising indicia comprising at least one of:

instructions for using the composition to treat a patient suffering from an anxiety disorder, or

instructions for using the composition to treat a patient suffering from depression, or

instructions for using the composition to treat a patient suffering from a sleeping disorder.

68. (Amended) A package comprising a pharmaceutical composition of claim [36] 53 in a container and further comprising indicia comprising at least one of: instructions for using the composition to treat a patient suffering from Alzheimer's dementia or instructions for using the composition to enhance cognition in a patient.

69. (Amended) A package comprising a pharmaceutical composition of claim [37] 53 in a container and further comprising indicia comprising at least one of:

instructions for using the composition to treat a patient suffering from an anxiety disorder, or

instructions for using the composition to treat a patient suffering from depression, or

instructions for using the composition to treat a patient suffering from a sleeping disorder.

70. (Amended) A package comprising a pharmaceutical composition of claim [37] 53 in a container and further comprising indicia comprising at least one of: instructions for using the composition to treat a patient suffering from Alzheimer's dementia or instructions for using the composition to enhance cognition in a patient.